UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,946	10/07/2002	Richard J Roman	650053--.91533	8704

7590 07/14/2005

Zhibin Ren
Quarles & Brady
411 East Wisconsin Aveneu
Suite 2040
Milwaukee, WI 53202-4497

EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,946	ROMAN ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *6,12,13 and 22-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11 and 14-21* is/are rejected.

7)☒ Claim(s) *1-5,8,9,11,14-18 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0502;1002*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election, with traverse, of Invention I, Claims 4-26, and HET0016 (A) in their response of June 17, 2005 is acknowledged. The traversal is on the following grounds. (i) Groups I and II relate to a single inventive concept of treating cerebral vascular disease by reducing 20-HETE synthesizing enzyme activity. Alonso-Galicia et al, 1997 relates to 20-HETE production in renal cortical microsomes and, therefore, does not anticipate the instant invention. (ii) Restriction requirements are optional and examination of Groups I and II can be performed without undue burden.

These arguments are not found to be persuasive for the following reasons. (i) It is acknowledged that Alonso-Galicia et al, 1997 relates to 20-HETE production in renal cortical microsomes. However, Alonso-Galicia et al, 1997 also teach that dibromododecenyl methylsulfimide inhibits the effects of nitric oxide on cerebral vasodilation (pg 324, parg 8). Moreover, Schimidt et al, 2000 teach that treatment with 1-aminobenzotriazole reduces the synthesis of 20-HETE (Fig 1) and reduces blood pressure (Fig 9), which is a well-known means to treat cerebral vascular diseases (see rejection under 102(b) below). Therefore, Groups I and II do not share a special technical feature, as treating cerebral vascular disease by reducing 20-HETE synthesizing enzyme activity was known in the art. (ii) It is acknowledged that inventions of Groups I and II are related. However, 35 U.S.C. 121 allows restriction of inventions that are independent or distinct. Since the methods of Groups I and II use different reagents, have different steps, and cause different results, the methods of said groups are distinct inventions. Searching Group I would not encompass searching Group II, or vice versa, and searching both

groups would be a burden on the Office. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-36 are pending. Claims 6, 12, 13, 22-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 4, 5, 7-11 and 14-21, as well as Claims 1-3 in so far as they encompass Invention I(A), are examined on their merits.

Specification-Objections

The title is objected to for not being descriptive of the elected invention, a method of treatment using HET-0016.

The abstract is objected to. The title page of a prior publication is no longer accepted as an abstract. A separate sheet, containing only the abstract, should be submitted.

Claims-Objections

The claim set is objected to for not beginning with a sentence of which the claims are an object e.g., "We claim" or "The claims are".

Claims 1-5 and 14-18 are objected to for reciting non-elected subject matter.

Claims 2, 3, and 5 are objected to for improper Markush language. For example in Claim 2, "is selected from occlusive strokes, hemorrhagic strokes, migraine headaches, cerebrovasospasm, infections, conditions caused by traumatic head and brain injury, and chronic neurological diseases associated with reduced blood flow" should be amended to "is occlusive strokes, hemorrhagic strokes, migraine headaches, cerebrovasospasm, infections, conditions caused by traumatic head and brain injury, or chronic neurological diseases associated with reduced blood flow" or "selected from the group consisting of occlusive strokes, hemorrhagic

strokes, migraine headaches, cerebrovasospasm, infections, conditions caused by traumatic head and brain injury, and chronic neurological diseases associated with reduced blood flow". Claims 3 and 5 should be amended in an analogous manner.

Claims 8, 9, 11, and 21 are objected to because in each said claim, "the dose" has no antecedent basis.

Claim 18 is objected to for not ending in a period (.).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 and 18 are rejected under 35 U.S.C. 101 because the claimed recitation of a process, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Double Patenting

> The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
> A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).
> Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the

reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Claims 1-5, 7-11, and 14-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-5, 7-11, and 14-21 herein and Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695 are both directed to methods of treatment using a 20-HETE synthesizing enzyme inhibitor. The claims differ in that Claims 3, 13, 21, and 28 of 10/986,695 recite methods using inhibitors that are not recited herein, while Claim 5 herein recites methods using inhibitors that are not recited in 10/986,695. The portion of the specification in 10/986,695 that supports the recited methods includes embodiments that would anticipate Claims 1-5, 7-11, and 14-21 herein, e.g., methods of treatment using a 20-HETE synthesizing enzyme inhibitor, which are also the methods specifically recited in Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695. Claims 1-5, 7-11, and 14-21 herein cannot be considered patentably distinct over Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695 when there are specifically recited embodiments (methods of treatment using a 20-HETE synthesizing enzyme inhibitor) that would anticipate Claims 1-5, 7-11, and 14-21 herein. Alternatively, Claims 1-5, 7-11, and 14-21 herein cannot be considered patentably distinct over Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695 when there are specifically disclosed embodiments in 10/986,695 that supports Claims 1-4, 6-13,

19-22, and 24-28 of that application and falls within the scope of Claims 1-5, 7-11, and 14-21 herein, because it would have been obvious to a skilled artisan to modify the methods of Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695 by selecting a specifically disclosed embodiment that supports those claims, i.e., methods of treatment using a 20-HETE synthesizing enzyme inhibitor, as disclosed in US Application No. 10/986,695. One having ordinary skill in the art would have been motivated to do this because using a 20-HETE synthesizing enzyme inhibitor for treatment of cerebral vascular diseases, which is known in the art (Alonso-Galicia et al, 1999 or Su et al, 1999), is disclosed as being a preferred embodiment within Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695. Moreover, angiogenesis, as discussed in US Application No. 10/986,695 is known in the art to contribute to the cerebral vascular diseases discussed herein (Zhang et al, 2002; Kalaria et al, 1998).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7-11, 14-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 and 18 provides for a method of treatment, but, since the claims do not set forth any steps involved in the method, it is unclear what method applicant is intending to

encompass. A claim is indefinite where it merely recites a method without any active, positive steps delimiting how this method is actually practiced.

Claim 4 recites administering a 20-HETE synthesizing enzyme inhibitor into an animal. However, Claim 4 is dependent from Claim 1, wherein treatment of a human and/or a non-human animal is recited. Therefore, it is not clear whether Applicant's intention is to recite treatment of a human or a non-human animal in Claim 4. Clarification is requested. Claims 5, 7-11, 14-17, as dependent from Claim 4, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite, for the same reasons.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

In this regard, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art.

Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 1-5, 7-11, and 14-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for intravenous administration of HET0016 to increase cerebral blood flow after subarachnoid hemorrhage and to decrease infarct volume following transient occlusion of the middle cerebral artery in rats, does not reasonably provide enablement for all methods of treating any cerebral vascular disease in any animal using any compound that decreases the activity of any 20-HETE synthesizing enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1 and 4, and 14-17 are so broad as to encompass any method of treating any cerebral vascular disease in any animal using any compound that decreases the activity of any 20-HETE synthesizing enzyme. Claims 2, 3, and 18 are so broad as to encompass any method of treating specific cerebral vascular diseases in any animal using any compound that decreases the activity of any 20-HETE synthesizing enzyme. Claims 5 and 7-11 are so broad as to encompass any method of treating any cerebral vascular disease in any animal using HET0016. Claims 19-21 are so broad as to encompass any method of treating subarachnoid hemorrhage in any animal using HET0016. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of methods broadly encompassed by the claim. Since the pharmaceutical agent, formulation, administration route, target population, and disease to be treated all determines the functional properties of any method of treatment, predictability of which changes can be tolerated in any method's process

and still and obtain the desired efficacy of treatment requires a knowledge of and guidance with regard to which pharmaceutical agents, formulation, administration route, if any, are tolerant of modification and which must be conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the method's process relates to its function as a treatment for any specific patient and/or disease. However, in this case the disclosure is limited to intravenous administration of HET0016 to increase cerebral blood flow after subarachnoid hemorrhage and to decrease infarct volume following transient occlusion of the middle cerebral artery in rats.

While methods of testing for treatment of any specific cerebral vascular disease in any animal using any compound, any formulation, and any administration route are known, it is not routine in the art to screen multiple compounds, multiple formulations, and multiple administration routes on multiple animals for treatment of multiple cerebral vascular diseases. Furthermore, the steps and reagents to be used with a reasonable expectation of success in obtaining the desired successful treatment of any specific disease are limited and may be unpredictable (del Zoppo et al, 1998). In addition, one skilled in the art would expect any tolerance to modification of any successful treatment method to diminish with each further and additional modification of steps and reagents used

The specification does not support the broad scope of Claims 1 and 4, and 14-17, which encompass any method of treating any cerebral vascular disease in any animal using any compound that decreases the activity of any 20-HETE synthesizing enzyme. The specification does not support the broad scope of Claims 2, 3, and 18, which encompass any method of treating specific cerebral vascular diseases in any animal using any compound that decreases the

activity of any 20-HETE synthesizing enzyme. The specification does not support the broad scope of Claims 5 and 7-11, which encompass any method of treating any cerebral vascular disease in any animal using HET0016. The specification does not support the broad scope of Claims 19-21, which encompass any method of treating subarachnoid hemorrhage in any animal using HET0016. The specification does not support the broad scope of Claims 1-5, 7-11, and 14-21 because the specification does not establish: (A) all cerebral vascular diseases that can be successfully treated with an inhibitor of 20-HETE synthesizing enzyme; (B) all enzymes that are 20-HETE synthesizing enzymes; (C) the structure of all compounds that are inhibitors of any 20-HETE synthesizing enzyme; (D) how any said compound can and cannot be modified and still inhibit a 20-HETE synthesizing enzyme; (E) the structure of inhibitors of any 20-HETE synthesizing enzyme that can be successfully used for treatment of any cerebral vascular disease; (F) how any said inhibitor can and cannot be modified and still be successfully used for treatment of any cerebral vascular disease; (G) administration routes that can be used to successfully treat any animal with any inhibitor of any 20-HETE synthesizing enzyme for treatment of any cerebral vascular disease; (H) a rational and predictable scheme for modifying any compound, formulation, or administration route with an expectation of obtaining the desired treatment result; and (I) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of methods for treating any cerebral vascular disease in any animal using any compound that decreases the activity of any 20-HETE synthesizing

enzyme. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 1-5, 7-11, and 14-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of methods for treating any cerebral vascular disease in any animal using any compound that decreases the activity of any 20-HETE synthesizing enzyme. The specification teaches only a two representative species of such methods. Moreover, the specification fails to describe any other representative methods by any identifying characteristics or properties other than the functionality of treating any cerebral vascular disease in any animal using any compound that decreases the activity of any 20-HETE synthesizing enzyme. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Alonso-Galicia et al, 1999 (IDS). Alonso-Galicia et al teach that intracerebroventricular injection of dibromododecenyl methylsulfimide reduces cerebral blood flow (Fig 7). Therefore, Claims 1-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Alonso-Galicia et al, 1999.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Su et al, 1999, as evidenced by Fotherby et al, 1997 or Schmidt et al, 2000. Su et al teach that 1-aminobenzotriazole reduces the synthesis of 20-HETE (Fig 1) and reduces blood pressure (Fig 9), which, as is well known in the art, is an effective means to treat cerebral vascular diseases (Fotherby et al or Schmidt et al). Therefore, Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Su et al, 1999, as evidenced by Fotherby et al, 1997 or Schmidt et al, 2000.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Frisbee et al, 2000. Roman et al teach that cerebral vascular diseases, including cerebral vasospasm, stroke, and hypertension, and migraine, can be treated by blocking the effects of 20-HETE (pg 5, lines 1-4). Roman et al do not teach treatment of cerebral vascular diseases with an inhibitor of 20-HETE synthesis. Frisbee et al teach that treatment with 17-ODYA and dibromododecenyl methylsulfimide inhibits 20-HETE production (pg H1518, parg 4-5) and thereby reduces vascular vessel diameter (Figs 2, 4, 6, and 8). It would have been obvious to a person of ordinary skill in the art to use 17-ODYA or dibromododecenyl methylsulfimide for treatment of cerebral vascular disease. Motivation to do so is provided by Frisbee et al, wherein they state that elevated 20-HETE levels contributes to hypertension (pg H1524, parg 1), which is well known in the art to be a causative factor in cerebral vascular disease. The expectation of success is high, as 17-ODYA or dibromododecenyl methylsulfimide are known inhibitors of 20-HETE synthesis. Therefore, Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Frisbee et al, 2000.

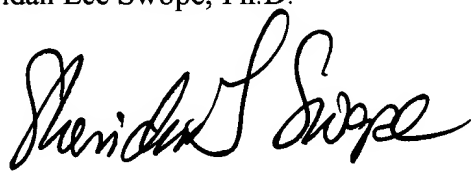
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.



AV1656